
Regulation of parkin and PINK1 by neddylation.

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Public Summary:

This study identifies a posttranslational modification of parkin and pink1. after modification, the E3 ligase activity of parkin/pink1 complex is increased. PD related neurotoxin MPP⁺ inhibits the type of modification and suppress the E3 ligase activity of parkin/pink1 complex.

Scientific Abstract:

Neddylation is a posttranslational modification that plays important roles in regulating protein structure and function by covalently conjugating NEDD8, an ubiquitin-like small molecule, to the substrate. Here, we report that Parkinson's disease (PD)-related parkin and PINK1 are NEDD8 conjugated. Neddylation of parkin and PINK1 results in increased E3 ligase activity of parkin and selective stabilization of the 55 kDa PINK1 fragment. Expression of dAPP-BP1, a NEDD8 activation enzyme subunit, in Drosophila suppresses abnormalities induced by dPINK1 RNAi. PD neurotoxin MPP⁽⁺⁾ inhibits neddylation of both parkin and PINK1. NEDD8 immunoreactivity is associated with Lewy bodies in midbrain dopaminergic neurons of PD patients. Together, these results suggest that parkin and PINK1 are regulated by neddylation and that impaired NEDD8 modification of these proteins likely contributes to PD pathogenesis.

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